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USSR REVIEW OF I. G. SHILLER'S BOOK ON DIRECTED ANTAGONISM OF BACTERIA

/Comment: The following is a summary of a review, by N. S. Yegorov and M. A. Popovskiy, of I. G. Shiller's book Directed Antagonism of Microbes (Napravlennyy Antagonism Mikrobov), published by the State Medical Publishing House of the Ukrainian SSR, 1952, 135 pages./

I. G. Shiller, who was I. I. Mechnikov's pupil, was the first to attain Mechnikov's goal of replacing the harmful bacteria of the human intestine with harmless microorganisms. The successful solution of this problem induced Shiller to pursue detailed studies on the antagonism of bacteria and the possibility of directing this antagonism into useful channels. Shiller published his first results on microbial antagonism in 1914. By 1923 he had developed a theory of enforced antagonism which he disclosed in USSR and foreign publications.

Shiller regards bacterial antagonism as an innate ability of a given species of microbes to kill microorganisms of another species or to suppress their activity. He succeeded in establishing that, under certain conditions of cultivation, antagonism can be induced in bacteria which, under normal conditions, do not exert any antagonistic effect. For instance, Bacillus mesentericus remains indifferent toward the streptococcus that produces purulent infections /Str. pyogenes?/ as long as both microorganisms live on a substrate which furnishes all the nutritive substances needed by them.

However, if the bacteria are placed in a medium that lacks nutritive substances (Shiller used distilled water for this purpose), one of the bacterial species (Bacillus mesentericus in this case), which has the capacity of evolving proteolytic enzymes, uses as nutrition the cells of the other species (streptococci in this case), which does not exert any proteolytic activity. Here we have antagonism that has been induced by the investigator. Shiller refers to it as enforced or provoked antagonism.

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Under conditions of nitrogen starvation, bacteria may use the cells of other living bacteria as nutrition only when they are capable of developing lysins which dissolve the cell contents of the other bacteria.

Schiller investigated the antagonist activity of a considerable number of proteolytic microorganisms, e. g., Bacillus mesentericus, Bacillus subtilis, Bacillus anthrax, various sarcinae, Staphylococcus albus, and Spathylococcus aureus. Hemolytic and nonhemolytic streptococci, Bulgarian /yoghurt?/ bacilli, Streptococcus lactis, and others were used as bacteria furnishing nutrition to the proteolytic microorganisms.

The lysins obtained by Shiller did not lose their capacity to dissolve bacterial cells even after the liquid that produced the lytic effect was freed of bacterial bodies and added to bacteria which were in a medium that supplied all the nutrient substances required by the bacteria. Shiller states that the lysins formed as a result of enforced antagonism are thermo-labile; after being heated for 2-3 hrs on a water bath at 56-57°, they lose their lytic properties. In this respect, the lysins are similar to enzymes.

Shiller further established that enforced antagonism may be induced not only when sources of nitrogen and carbohydrate nutrition are absent but also when a fully balanced nutritive substrate is present. Under these conditions cultivation must be carried out in such a manner that maximum activity is provided for one species of microorganisms, while the other species is condemned to a passive mode of existence.

There are two essential causes of the development of enforced antagonism: inadequate nutrition and interspecies competition brought about under the conditions of cultivation due to the necessity of self-protection of one species against supplantation by another. Shiller has not sufficiently clarified the problem as to whether trophic or protective functions play the leading role in the formation of lytic substances by bacterial antagonists. Further work on this subject is required.

Of great interest is Shiller's discovery that the antagonistic relationship between bacteria is biologically reversible. By appropriately modifying the conditions of the existence of the microorganisms, it was possible to transform an active antagonist into a nutritional substrate for a microorganism which prior to that served as a source of nutrition for the antagonist. For example, Shiller reports interesting data to the effect that he was able, at will, to obtain digestion of yeast by bacteria or of bacteria by yeast.

Shiller's conclusion that the biological properties of microbes can be modified within an extensive range, depending on practical needs, have been confirmed by successful work carried out by many Soviet microbiologists.

The investigations outlined in Shiller's book are not only of theoretical interest but also of great practical significance. The chapters on the practical utilization of chemical products that arise in connection with the development of enforced antagonism give information which is of considerable interest. The lysins evolved by bacteria in the process of digestion of living microbial cells are particularly promising from the standpoint of medical applications. Not being a biochemist, Shiller did not carry out a chemical analysis of the lysins. However, he investigated their antibiotic activity and pointed out their possible therapeutic uses. The bacterial lysins (originally isolated by Shiller in 1923) are the first known antibiotics. Shiller therefore deserves credit for the discovery of antibiotics 16-17 years earlier than the American Dubos /R. J. Dubos/ or the Englishman Florey /probably H. W. Florey/.

The phenomenon of enforced antagonism that has been discovered by Shiller furnished to science a promising method of preparing antibiotics which have a directed action /i.e., act in a predetermined manner/. The products developed by bacteria as a result of enforced antagonism have already received clinical recognition. Shiller's book cites extensive data on their application at the Odessa Dermatovenereological Institute for the therapy of severe hydroadenites, which are not susceptible to treatment by other means, and of persistent furunculosis. In stomatology these products proved effective for the treatment of pulpites brought about by streptococci and staphylococci. On the basis of Shiller's ideas, a group of workers at the Ukrainian Institute of Stomatology created the preparation Sol'vin, which has a destructive effect on streptococci and staphylococci.

A special chapter of Shiller's book is devoted to the forced feeding of bacteria with various animal cells. This work is of great importance both from the standpoint of theory and that of clinical applications. The theory that some pathogenic bacteria are saprophites which have adapted themselves to new conditions of existence in the human organism is familiar. However, it has not been made clear just what conditions contribute to the transformation of saprophites into pathogenic bacteria.

In Shiller's experiments, saprophitic bacteria (e.g., Bacillus mesentericus and some lactic acid bacteria) acquired the capacity to feed on muscle cells, erythrocytes, etc. In using these substrates, the bacteria developed specific substances the solvent power of which was directed selectively against the cells of some definite organ. When healthy animals received the lysins of Bacillus mesentericus evolved in the process of feeding of this microorganism on heart muscles of a mouse, the animals died because their hearts were impaired by the action of the lysin preparation. In commenting on these and similar experiments, Shiller remarks that the isolation of specific substances which dissolve animal cells creates a basis for experiments on the therapy of malignant tumors.

Shiller's book is distinguished by its concise style, its wealth of general biological information, its daring conclusions and generalizations, and, most important, its clarity of exposition in discussing one of the most important discoveries of native /i.e., Russian/ microbiology, that of enforced antagonism.

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